TβSR-ED is a TGF-β receptor type II ectodomain (TIβR-II-ED). In a preferred embodiment, the TβSR-ED comprises a sequence selected from the group consisting of SEQ ID NO:35, SEQ ID NO:69, SEQ ID NO:75, SEQ ID NO:81, and a sequence substantially identical thereto.

[0014] The second portion may comprise a sequence selected from the group consisting of SEQ ID NO:43-SEQ ID NO:51, SEQ ID NO:61-SEQ ID NO:68, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:88, and a sequence substantially identical thereto.

[0015] In a preferred embodiment, the first portion of a polypeptide construct of the present invention further comprises a C_{H1}, a C_{H1} and V_H, or C_{H1} and scFv.

[0016] There is provided a polypeptide construct of the present invention wherein the antibody heavy chain is of human origin. In a preferred embodiment, the antibody heavy chain is selected from the group consisting of a human IgG1, IgG2, IgG3, or IgG4 heavy chain. More preferably, the antibody heavy chain is a human IgG1.

[0017] In accordance with the present invention, the polypeptide construct shows longer in vivo half-life compared to the half-life of the second portion alone.

[0018] There is provided a polypeptide construct of the present invention, wherein the polypeptide construct is a single chain polypeptide.

[0019] In an embodiment, the polypeptide construct forms a dimeric polypeptide. In another embodiment, the polypeptide construct is heterodimeric.

[0020] There is provided a polypeptide construct selected from the group consisting of any one of SEQ ID NO:91 to SEQ ID NO:120, and a sequence substantially identical thereto.

[0021] There is provided a polypeptide construct according to the present invention, wherein the construct comprises an antibody, antigen binding fragment thereof, or a targeting moiety. In a preferred embodiment, the antibody, the antigen binding fragment, or the targeting moiety is at the N-terminus of the first portion.

[0022] In a preferred embodiment, the antigen binding fragment may be selected from the group consisting of a Fv, scFv, Fab, or sdAb. In a preferred embodiment, the antigen binding fragment binds to any antigen, provided that it is not PD-L1, EGFR1, Her-2, CD4, CD6, CD20, CD25, MUC-1, IL-2, IL-6, or CTLA-4.

[0023] In a preferred embodiment, a polypeptide construct of the present invention comprises an antibody selected from the group consisting of Cetuximab, Avastin, Herceptin, Synagis, and FC5. In a preferred embodiment, the antibody is Cetuximab.

[0024] In a preferred embodiment, a polypeptide construct of the present invention comprises a targeting moiety, wherein the targeting moiety comprises a poly-aspartate sequence motif for bone targeting. In a preferred embodiment, the targeting moiety comprises D10.

[0025] There is provided a polypeptide construct according to the present invention wherein the construct is a dimeric polypeptide; wherein the dimeric polypeptide comprises: a first single chain polypeptide comprising a first portion comprising the second constant domain (C_{H2}) and third constant domain (C_{H3}) of an antibody heavy chain, and a heavy chain variable region of a given antibody; a second portion comprising one or more TGF-β superfamily receptor ectodomains (TβSR-ED), wherein the N-terminus of the second portion is linked to the C-terminus of the first portion, and a second single chain polypeptide comprising a first portion comprising the second constant domain (C_{H2}) and third constant domain (C_{H3}) of an antibody heavy chain, and a light chain variable region of said given antibody; a second portion comprising one or more TGF-β superfamily receptor ectodomain (TβSR-ED) which is the same or different from the ectodomain(s) in the first polypeptide, wherein the N-terminus of the second portion is linked to the C-terminus of the first portion.

[0026] There is also provided a nucleic acid molecule encoding the polypeptide construct of the present invention. There is also provided a vector comprising the nucleic acid molecule of claim the present invention.

[0027] There is also provided a composition comprising one or more than one independently selected polypeptide construct of the present invention and a pharmaceutically-acceptable carrier, diluent, or excipient.

[0028] There is also provided a transgenic cellular host comprising the nucleic acid molecule or a vector of the present invention. The transgenic cellular host further comprising a second nucleic acid molecule or a second vector encoding a second polypeptide construct different from the first polypeptide construct.

[0029] There is also provided the use of a polypeptide construct according to the present invention for treatment of a medical condition, disease or disorder; wherein the medi medical condition, disease or disorder comprises, but is not limited to, cancer, ocular diseases, fibrotic diseases, or genetic disorders of connective tissue.

[0030] In a preferred embodiment, there therefore provided a polypeptide construct comprising:

[0031] a first portion comprising the second constant domain (CH2) and/or third constant domain (CH3) of an antibody heavy chain, and

[0032] a second portion comprising at least two TGF-β superfamily receptor ectodomains (TβSR-ED),

[0033] wherein the N-terminus of the second portion is linked to the C-terminus of the first portion.

[0034] The antibody constant domain can further comprise, either linked thereto or formed integrally therewith, a binding agent such as a full size antibody, a ligand or any other protein of interest. In the alternative, the antibody constant domain comprises only the CH2 and/or CH3 regions, and not a full size antibody. In these and other types of constructs, the CH2 and/or CH3 region can be altered by deleting or substituting amino acids including one or more of the cysteines that provide cross-linking when the present constructs are provided as dimeric constructs.

[0035] In other aspects of the present invention, there is provided a polypeptide construct that incorporates one or more such ectodomains. When the constructs comprise only one ectodomain linked to the antibody constant domain, then the construct is further characterized by at least one of the following: (1) when the constant domain further comprises a full sized antibody, that antibody does not bind effectively to PD-L1 or to an immunoregulatory antigen selected, (2) the constant domain comprises only the CH2 and/or CH3 regions, (3) the constant domain comprises an amino acid alteration relative to a wild type counterpart, such as a cysteine residue alteration; and (4) the first portion is linked to the second portion directly and without intervening amino acids.